Non-pharmacological interventions for the improvement of post-stroke quality of life amongst older stroke survivors: a systematic review of systematic reviews (The SENATOR ONTOP series)

Carrie Stewart[1,2¶] Selvarani Subbarayan[1,2¶] Pamela Paton[1¶] Elliot Gemmell[1¶] Iosief Abraha[3¶] Phyo Kyaw Myint[1,2¶] Denis O'Mahony[4¶] Antonio Cherubini[3¶] Alfonso J Cruz-Jentoft [5¶] Roy L Soiza[1,2¶]

[1]Department of Old Age Medicine, Aberdeen Royal Infirmary, Aberdeen, U.K.

[2] Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, U.K.

[3]Geriatria, Accettazione geriatrica e Centro di ricerca per l'invecchiamento, IRCCS INRCA, Ancona, Italy.

[4]Department of Geriatric Medicine, University College Cork, Cork, Ireland.

[5]Fundación para la Investigación Biomédica del Hospital Universitario Ramón y Cajal, Madrid, Spain.

[*]Corresponding author:

Dr. Carrie Stewart

Email: carrie.stewart@abdn.ac.uk **(CS)**

Telephone: +44(1224) 437144

ORCID

CS 0000-0002-2325-3380

SS 0000-0002-0322-9244

PP 0000-0001-7723-4698

EG 0000-0003-4749-6704

IA 0000-0002-5440-775

PKM 0000-0003-3852-6158

DOM 0000-0003-2236-5222

AC 0000-0003-0261-9897

AJC 0000-0001-7628-4861

RLS 0000-0002-1397-4272

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Abstract

Purpose

The efficacy of non-pharmacological stroke rehabilitation approaches for older stroke survivors is largely unknown, particularly in relation to psychosocial outcomes such as quality of life. This systematic review examined the evidence for such interventions as part of the Optimal Evidence-Based Non-Drug Therapies in Older Persons (ONTOP) project conducted under an European Union funded project called the Software Engine for the Assessment and Optimisation of Drug and Non-Drug Therapies in Older Persons (SENATOR) [http://www.senator-project.eu].

Methods

Thirteen experts in geriatric medicine, as part of a Delphi panel, agreed quality of life to be a critical outcome of stroke rehabilitation. A comprehensive search strategy was developed and databases were searched for eligible systematic reviews from which trials meeting our criteria were identified. Eligible papers were then double reviewed. Due to heterogeneity, narrative analysis was performed. Cochrane risk of bias and GRADE assessment tools were used to assess bias and quality of evidence.

Results

We identified 28 trials, spanning ten types of intervention. Limited evidence supports the use of additional occupational therapy and physiotherapy, with very limited evidence supporting our recommendation to explore caregiver training, constraint induced movement therapy, device assisted physiotherapy, and self-management education further.

Conclusion

Limited evidence suggests a range of non-pharmacological interventions may improve the quality of life of older stroke survivors. However, evidence is limited by low study quality and the small number of studies targeting older stroke survivors. We recommend future studies explore such interventions exclusively in older adult populations and improve methodological and outcome reporting.

Keywords

Older Adults; Ageing; Stroke; Rehabilitation; Non-pharmacological Therapies

Introduction

While survival from stroke continues to increase, many survivors experience some degree of post-stroke impairment or disability, most frequently affecting limb use, mobility, speech, and cognitive functions [1]. Psychosocial consequences resulting from such impairments has been associated with low mood, depression, and reduced quality of life (QOL) [1]. Therefore, effective rehabilitation, which can reduce post-stroke impairment and restore a person's functional abilities, is imperative to enhance the survivors' psychosocial wellbeing.

Stroke guidelines recommend multi-disciplinary rehabilitation teams, reflecting the diverse physical, psychological and social rehabilitation needs of patients post-stroke [2-4]. While occupational therapy (OT) and physiotherapy (PT) have become commonplace in the rehabilitation of stroke survivors, an array of other non-pharmacological interventions have been suggested to be beneficial [3]. However, the evidence base for such interventions can be conflicting and inconclusive [3]. Several factors can influence the success of rehabilitation including stroke severity, the type and location of a stroke, and the patient's general health [5]. Age is also highly influential: older patients are at a higher risk of poorer outcomes [6]. Additionally, the effectiveness of such interventions within the older stroke population is largely unknown. Much of the literature exploring the efficacy of post-stroke rehabilitation interventions involves younger adults [7]. Therefore, many stroke intervention trials may not be representative of typical stroke survivors, or specifically, older stroke survivors.

Despite current uncertainties, non-pharmacological approaches to treat post-stroke impairments are preferred for older patients. Older people are at an increased risk of adverse drug reactions (ADR) resulting from multiple co-morbidities, polypharmacy, poor adherence to medication regimens, and age-related changes in pharmacokinetics and pharmacodynamics [8]. Moreover, polypharmacy might

negatively affect the outcomes of stroke rehabilitation [9]. Therefore, there is a compelling case to understand the efficacy of non-pharmacological treatments for older stroke survivors. This systematic review aimed to identify expert agreed critical outcomes for stroke interventions and review the evidence for such interventions in patients aged 65 years and older. One identified outcome (as described in methods) was that of QOL, the results of which are presented in this manuscript. This systematic review was conducted as part of the Optimal Evidence-Based Non-Drug Therapies in Older Persons (ONTOP) project [10-11] and a number of our reviews have been completed, including for pressure ulcer risk reduction and treatment [12] and fall prevention [13]. ONTOP is in turn part of a larger, European Union (EU) funded project called the Software Engine for the Assessment and Optimisation of Drug and Non-Drug Therapies in Older Persons (SENATOR) [http://www.senator-project.eu]. Recommendations from ONTOP reviews are intended for use in the SENATOR project to produce a software programme that can advise clinicians on the use of pharmacological and non-pharmacological therapies in older persons, while limiting the risk of polypharmacy and ADRs [11].

Methods

The systematic review methodology was developed specifically for the ONTOP project. Fig 1 presents an outline of the stages this methodology involved. In summary, the methodology was devised to capture primary studies, RCTs or quasi-RCTs, from published systematic reviews. This process was followed in this review of non-pharmacological interventions for the treatment of older stroke survivors. Outcomes were determined by consensus opinion using the Delphi approach, as described below. The review protocol has not been registered but has been published [10], and findings will be published in accordance with PRISMA reporting standards [10]. See Online Resource 1 for the PRISMA checklist.

Fig 1. ONTOP Review Methodology

Delphi process

Outcomes were selected by a panel of 13 European experts in geriatric medicine and methodology using a Delphi process, a structured, questionnaire-based method of reaching consensus [14]. A literature review generated a list of all outcome measures used in stroke research that was then given to panellists as a questionnaire. Panellists, anonymously, rated each outcome from 1-9 according to their perception of its clinical importance. The mean score for each outcome was then used to categorise outcomes by importance: not important (score of 1-3), important but not critical (score of 4-6), and critically importance (7-9). These boundaries were selected based on the Grading of Recommendations, Development and Evaluation (GRADE) method for evaluating the quality of evidence [15]. Panel members could suggest additional outcomes for consideration if they felt that an important outcome had been overlooked. Outcomes ranked as critical were used for this review.

Activities of daily living (ADL), QOL and disability were the only outcomes rated as being critically important. In this paper we present the results for quality of life only. The results for ADL and disability have been published separately [16].

Literature search strategy

A search strategy (Fig 1) was designed based on Montori's highly specific search strategy for retrieving systematic reviews from PubMed [17]. This search strategy was then modified for use in other databases. In total, five databases were searched (Cinahl, Cochrane Database of systematic Reviews, Embase, PsycInfo, PubMed) without restrictions on publication status or date. The search strategy is presented as supplementary material (Online Resource 2). The searches were conducted in December 2015 and updated April 2018.

Inclusion criteria

The following criteria were used:

Systematic reviews

- Full text was available in English, Spanish or Italian.
- Identified at least one primary study matching this review's inclusion criteria.
- Specifically mentioned conducting a search of at least one medical literature database.
- Guidelines were also considered for inclusion provided that they used a transparent and systematic approach to retrieve the evidence.

Primary studies

- All participants must be ≥65 years of age, or the mean age of participants must be ≥65 years of age
- All aetiologies, types and severity of stroke/ stroke symptoms included
- Involves any non-pharmacological intervention for stroke:
    a. a single or multi-component non-drug intervention used to improve symptoms post-stroke
    b. a non-drug intervention being a treatment or therapy that can be performed on or given to a patient, and/or taught to the patient for them to practice themselves.
    c. A non -drug intervention which is deliverable in clinical practice
- Treatment for any complications or specific disability of stroke (e.g. urinary incontinence, shoulder subluxation, neglect syndrome etc.) will be included **if** the study reports ≥1 relevant outcome
- Compares the non-pharmacologic treatment against no treatment, a sham intervention or a treatment considered standard practice at the time of the study.
- A study using Randomised Controlled Trial (RCT) or Quasi RCT methodology
- Paper must focus on at least one or more of three Delphi consensus derived outcome variables: ADL, quality of life or disability (total global/ multi-domain scores only).
- Papers published only in English, Italian and Spanish

Exclusion criteria

Primary studies

- Any therapy for *stroke prevention*
- Any therapy using non-conventional products but administered in a conventional route (e.g. Chinese medicine, herbal supplements)
- Observational or before-after studies with historical controls
- The inclusion of participants with other neurological conditions
- Studies exploring the management of stroke in critical care/ Accident &Emergency
- Health services research evaluating the two different stroke units (hospital based, community or home-based), two or more different methods of delivering non-pharmacological therapy (e.g. face to face or telephone rehabilitation), or evaluating different methods of delivering/ co-ordinating discharge care (e.g. named person in charge of discharge/ post-discharge care versus usual care)
- Economic evaluations of non-pharmacological therapy
- Papers discussing the dose-response relationship (duration, intensity of therapy or time to commence treatment, including early discharge)
- Interventions which only involve the provision of education/ stroke information and general sign posting/ liaison with other services where the patient plays a passive role (NB: If these components are included in a broader structured multi-component intervention such as a self-management programme the intervention will be included).

Study selection

For this review, 18,932 potentially relevant articles were identified from database searches (Fig 2). After removing duplicates, 13,627 unique records were screened by title and abstract by two reviewers. Only 363 full texts of systematic reviews were deemed eligible based on their abstracts. Of

these, 173 reviews matched the eligibility criteria and were read in full, and their references were hand searched to identify potentially relevant primary studies. The initial searches were conducted in December 2015, with no restrictions on publication date, and resulted in 83 primary articles for inclusion. The review was updated as above in April 2018 and a further six papers were added to the findings.

Fig 2. Study Selection Process

Data collection

The results of the database searches were amalgamated using Refworks 6.0 software (ProQuest LLC, USA). A list of the titles and abstracts of systematic reviews were screened by two independent assessors (EG, CS). Any disagreements over eligibility were resolved through discussion with other members of the research team (RS and PKM).

The full-text articles of potentially eligible reviews and meta-analyses were then retrieved and assessed for eligibility, again by two independent assessors (EG and CS). The references of the included studies in eligible systematic reviews were hand-searched to identify primary studies relevant to this review. A list of the titles and abstracts of potentially eligible primary studies was screened (EG, CS, SS, RS and PKM). Thereafter, the full-text articles of potentially relevant primary studies were retrieved and screened by EG and CS.

Data extraction

A data extraction form was designed by adapting the Cochrane Collaboration's Data Extraction and Assessment Template. The information contained on the data extraction forms (study methodology, participant characteristics, and outcome data) was then transferred to an Excel spreadsheet for narrative analysis. Results were also transferred to RevMan 5.3 [Cochrane Collaboration, UK, http://community.cochrane.org/help/tools-and-software/revman-5] to facilitate risk of bias tables. Results were also transferred to the GRADE Pro online system [http://www.gradeworkinggroup.org] for the development of recommendations for each type of non-pharmacological intervention. Types, or categories, for non-pharmacological interventions were developed and applied to organise the included studies into meaningful categories of interventions for the analysis. Data extraction was performed by two independent assessors (CS & EG).

Risk of bias

Risk of bias was assessed using the Cochrane Collaboration's Risk of Bias tool [18]. This tool assesses: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. A decision was made as to whether the risk of bias for each category should be described as low, unclear or high risk. The overall risk of bias for the study was then judged by taking account of the assessments for each individual category. Results from the risk of bias assessment were entered into RevMan 5.3 software to enable the production of risk of bias graphs and summary tables.

Development of PICO questions

Clinical questions were formulated using the PICO (Population, Intervention, Comparator, and Outcome) framework for each intervention type and outcome assessed. Due to the small number of

papers in each category of intervention, the PICO questions chosen were considered to be the most pertinent and inclusive questions. For most categories of intervention one question assessing the efficacy of intervention types upon each outcome was chosen. As physiotherapy and occupational therapy are often standard care in stroke rehabilitation, studies investigating these therapies had no control intervention. Therefore, we split physiotherapy and occupational therapy studies depending upon whether they compared a more intensive (increased time and duration) of therapy against usual intensity, or if they compared two or more different forms of therapy.

Narrative analysis

All primary studies were included in a narrative assessment. The effects reported in each study were described as favouring the intervention, favouring the control, or as showing no significant difference. The overall findings of the studies were assessed qualitatively considering methodological quality and risk of bias. Patterns of effect across the studies were described and possible reasons for effect differences between studies explored, as per guidance offered by the ESRC [19]. Due to substantial clinical heterogeneity between studies and poor study reporting, meta-analysis of results was not considered appropriate. Clinical heterogeneity was assessed qualitatively by all authors and focused upon intervention content, target (e.g. upper or lower limb impairment), delivery, duration.

Assessing quality of evidence

After the completion of analysis, evidence for each non-pharmacological category was assessed using the GRADE method [15]. The GRADE approach assesses the evidence across all studies analysed for a given outcome, rather than assessing the evidence from each study individually. The GRADE framework allows the quality of the body of evidence, and consequentially any recommendations to

be made from this evidence, to be judged across five criterions known to limit the quality of evidence. Further details regarding each of these criteria can be found on the GRADE website [http://www.gradeworkinggroup.org]. The quality of the evidence was assigned an overall rating of quality, as described below in Table 1.

Table 1 GRADE Evidence Rating Descriptions

Quality Level	Description
High quality	*Further research is very unlikely to change our confidence in the estimate of effect*
Moderate quality	*Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate*
Low quality	*Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate*
Very low quality	*Any estimate of effect is very uncertain*

Development of recommendations

After the quality of evidence had been determined, concise recommendations were developed regarding the use of non-pharmacological therapies after stroke in older persons. These recommendations were written taking account of the quantity, quality and GRADE score of the available evidence.

Results

Of 89 retrieved articles examining the impact of a non-pharmacological intervention upon older stroke survivors, 28 papers reported QOL as an outcome measure. Results are presented in the sections below, organised by the types of non-pharmacological intervention; Acupuncture (n=2), Caregiver Training (n=1), Constraint Induced Movement Therapies (n=1), Device-assisted Physiotherapy (n=1), Music Therapy (n=1), Nerve Stimulation (n=2), Occupational Therapy (n=3), Physiotherapy (n=11), Self-management Education (n=5) and Videogames (n=1). Online Resource 3 presents the reference list of all included studies, and Online Resource 4 provides a more detailed description of each included intervention.

Acupuncture

Studies

Two studies were included in this category; both were conducted as RCTs, one within the UK and one within Sweden [20-21].

Participants

In total, 266 participants were involved in these studies, of which 150 (56.4%) were male. Participants' characteristics across the included studies are presented in table 2.

Interventions

Interventions varied in their design (for example number of acupuncture points used or whether manual or electrical stimulation was applied) and in their duration. Intervention descriptions are summarised in table 2.

Risk of Bias

Both studies adequately blinded participants and outcome assessors, but the methods of randomisation and allocation concealment were unclear for one study.

Table 2 Participant Characteristics and Study Descriptions of Included Acupuncture Studies

Study	Arm	No. of Participants	Male/ Female	Age (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
Johansson 2001 [20]	I1	150	90/60	76.0 (9.0)	NR	Acupuncture needles, 15 and 30 mm, and the Cefar Acus stimulator were used. Two modes of treatment were alternated (with either 10 or 9 acupuncture points). The non-electro-stimulated needles were manipulated.	Two 30-minute sessions per week	10 weeks
	I2			77.0 (9.0)		TENS was given to participants with the Cefar dual TENS stimulator and adhesive electrodes. Only the effected side was stimulated.	Two 30-minute sessions per week	10 weeks
	C			76.0 (11.0)		For subliminal stimulation the same equipment and placements of electrodes were used as in the TENS group but were given below the perception threshold (no skin sensation and no visible muscle contractions).	Two 30-minute sessions per week	10 weeks
Park 2005 [21]	I	116	60/56	74.8 (10.0)	NR	Manually stimulated acupuncture using standard needles at recognised points based on Korean medicine. 10 needle points used, 6 tailored to participant and 4 standard for stroke. Participants also received routine rehabilitation care.	Nine to twelve 20-minute sessions	2 weeks
	C			74.1 (10.2)		Sham treatment using non-penetrating needles 1.5cm away from recognised points. Participants also received routine rehabilitation care.	Nine to twelve 20-minute sessions	2 weeks

C: Control I: Intervention I1: Intervention arm 1 I2: Intervention arm 2 NR: Not Reported SD: Standard Deviation TENS: Trancutaneous Electrical Nerve stimulation

What is the effectiveness of acupuncture upon older stroke survivors QOL scores in comparison to usual rehabilitation care without acupuncture or sham treatment?

Two studies reported the impact of an acupuncture intervention upon QOL scores [20-21], as presented below in table 3. Neither study identified significant benefit upon older stroke survivors QOL scores arising from an acupuncture intervention. Johansson *et. al.* (2001) measured Nottingham Health Profile (NHP) scores at three and 12-months post-intervention, and found no statistically significant differences between groups for total NHP score or any of the subsections of the questionnaire (p-values and confidence intervals not reported) [20]. Similarly, Park *et. al.* (2005) using the both the EQ5D and EQVAS at 2 weeks post-intervention found no between group difference in either scores [21]. A GRADE quality assessment found the evidence to be of low quality (see table 3) because of heterogeneity between the two trials and the small sample size. This means that further studies are very likely to impact upon the findings of this review.

Table 3 Results of Studies Investigating Acupuncture upon Older Stroke Survivors QOL Scores

Study	Intervention		Control	p-value	GRADE Score	GRADE Comment
Johansson 2001 [20]	Acupuncture NHP (Median, IQR) Base: NR 3mths: 27 (16–39) 12mths: 28 (8–42)	TENS NHP (Median, IQR) Base: NR 3mths: 30 (17–46) 12mths: 34 (16–47)	Sham NHP (Median, IQR) Base: NR 3mths: 34 (18–50) 12mths: 32 (24–47)	NHP p =ns	⊕⊕◯◯ LOW	a. The variation in intervention design, delivery and duration suggests high heterogeneity between trials. b. Small overall sample size
Park 2005 [21]	EQ5D (Median, IQR) Base: NR 2wks: 0.64 (0.03-0.8) EQVAS (Median, IQR) Base: NR 2wks: 60 (48.6-72.5)		EQ5D (Median, IQR) Base: NR 2wks: 0.64 (0.09-0.71) EQVAS (Median, IQR) Base: NR 2wks: 50 (49.6-70)	EQ5D p =ns EQVAS p =ns		

Base: Baseline EQ5D: European Quality of Life 5 Dimensions EQVAS: European Quality of Life Visual Analogue Scale IQR: Inter-quartile Range Mths: Months NHP: Nottingham Health Profile NR: Not Reported NS: Not Significant Wks: Weeks

Caregiver Training

Studies

Only one study investigated the effect of caregiver training upon older stroke survivors QOL. The RCT by Kalra *et. al.* (2004) was conducted within an inpatient rehabilitation unit in one UK hospital [22].

Participants

The study involved 300 participants, 53% of whom were male. The intervention group had a median age of 76 years (IQR 70-80) versus a control group median of 76 years (IQR 70-82). The time between stroke onset and the intervention was not reported.

Intervention

Caregiver training consisted of three to five 30 to 45 minute sessions of instruction on common stroke related problems, their prevention and management, and hands on training in moving and handling, mobility encouragement, transfers, and speech/ communication [22]. Sessions were commenced in the hospital whilst the participant was an inpatient [22]. One final session was delivered to the caregiver in the participant's home environment following participants discharge. Control participants received usual care only [22].

Risk of Bias

A lack of blinding represents the most significant risk of bias for this study [22].

Can pre-discharge caregiver training effect post-discharge stroke survivors' quality of life scores in comparison to those who receive no caregiver training?

Kalra *et. al.* (2004) investigated if caregiver training prior to participant discharge could affect participant QOL post discharge [22]. At three months post-intervention, intervention participants scored a median of 60 (42-70) on the EuroQOL (European Quality of Life) versus a median of 50 (40-90) of the control participants (p= 0.019) [22]. At 12 months, intervention participants median score increased to 65 (IQR 55-80) versus the control groups 60 (IQR 41-80), with the difference between the two groups being significant (p=0.009) [22]. The findings suggest that stroke survivors whose caregivers had received training reported higher QOL scores than those whose caregivers had not received training. However, the evidence base has been GRADE assessed as being of low quality and therefore further studies are likely to change the expected effect.

Constraint Induced Movement Therapy

Studies

Only one study was included in the category of Constraint Induced Movement Therapy (CIMT). The study by Wu *et. al.* (2007) was an RCT conducted in outpatient occupational therapy departments in Taiwan [23].

Participants

The trial randomised 26 participants who had a mean age of 72 years. Fifteen participants were male and the mean time since stroke across the sample was 7.5 months.

Intervention

The study by Wu *et.al.* (2007) involved a three-week comparison between a modified CIMT technique and traditional rehabilitation [23]. Modified CIMT subjects placed their unaffected hands in self-adhesive strapping for six hours per day while at home [23]. Additionally, participants received two hours of CIMT with a therapist for five days per week [23]. Control participants followed a traditional ADL rehabilitation programme [23].

Risk of Bias

Unblinded participants and a lack of clarity surrounding allocation concealment both raise potential sources of bias [23].

What is the effectiveness of CIMT upon older stroke survivors QOL scores in comparison to those receiving conventional rehabilitation only?

The study assessed QOL using the Stroke Impact Scale (SIS). Intervention participants improved their SIS scores from a baseline mean of 53.13 (8.95) to 62.22 (8.71) versus control participants baseline mean of 63.70 (14.95), which had changed very little at follow up with a mean of 63.64 (15.18) [23]. The CIMT intervention had a large beneficial effect on QOL, with a significant effect size measured using the r statistic of 0.59 (p=0.001) [23]. However, due to a lack of studies, very small sample size, unblinded participants and poor reporting of methods, the GRADE assessment of the body of evidence was assessed as being low quality. Therefore, a recommendation to utilise CIMT for post-stroke rehabilitation is based on very limited evidence.

Device assisted physiotherapy

Studies

Only one trial investigating the impact of device assisted physiotherapy upon QOL was identified. It was conducted as a three-arm RCT in the USA [24].

Participants

The trial involved 127 older stroke survivors, of whom 122 (96%) were male. Time between stroke and intervention was on average 3.6 (4.0) years.

Interventions

The 3-arm study by Lo *et.al*. (2010) compared a robotic upper limb device against intensive upper limb therapy and a control group of usual care [24]. The robotic system consisted of four modules: a shoulder–elbow unit; an antigravity unit; a wrist unit; and a grasp- hand unit [24]. Modules were used to perform high-intensity, repetitive, task-oriented movements, directed by video screens [24]. Intensive comparison therapy consisted of a structured protocol using conventional rehabilitative techniques [24]. Both interventions were delivered for a maximum of 36 sessions over 12 weeks [24]. Control participants received usual care only [24].

Risk of Bias

Unblinded participants combined with a lack of information regarding methods of randomisation and allocation concealment presents a risk of bias regarding the findings of this study [24].

What is the effectiveness of a robotic PT device upon older stroke survivors QOL scores in comparison to those receiving conventional PT rehabilitation?

Regarding the effect of robotic devices on QOL, only one study reported relevant results. Lo *et.al.* (2010) conducted a 3-arm study comparing robot-assisted therapy, intensive therapy and usual care delivered over 12 weeks [24]. Using the SIS they reported a statistically significant difference in means of 7.64 favouring the group that received robot therapy (95%CI [2.03; 13.24], p=.009) versus usual care [24]. However, the difference in means between the robotic therapy and intensive therapy was not significant (p=.81) [24]. Therefore, robotic therapy did not benefit stroke survivors any better than intensive therapy, but may benefit stroke survivors QOL against usual care. However, the GRADE quality assessment score was low due to the lack of studies and small sample size. Therefore, the evidence supporting therapy for stroke rehabilitation is very limited.

Music Therapy

Studies

One study investigated the role of music therapy in the treatment of older stroke survivors QOL. The RCT was conducted in Italy [25].

Participants

The trial by Raglio *et. al.* (2017) involved 38 participants, 16 (42.1%) of whom were male [25]. The time between stroke and intervention for all participants was between six and eight weeks.

Interventions

Intervention participants participated in Relational Active Music Therapy, conducted by trained musical therapists [25]. Participants were encouraged to use rhythmical instruments during these sessions, which were delivered three times per week for up to twenty sessions [25]. Control participants received no additional intervention [25].

Risk of Bias

Unblinded participants and insufficient information regarding methods of randomisation and allocation concealment [25] present the most important risks of bias in relation to the findings of this study.

What is the effectiveness of music therapy upon stroke survivors QOL against usual care alone?

Raglio *et. al.* (2017) investigated if participation in music therapy would benefit older stroke survivors QOL [25]. While both intervention and control participants improved over time (p=.04) there was no significant difference between the groups final scores or change in score from baseline [25]. Based upon one small study (n=38), with an unclear risk of bias, which demonstrated no improvement in QOL, we cannot recommend the use of music therapy to improve QOL amongst older stroke survivors.

Using the GRADE system the results suggest the evidence is of low quality, meaning that further studies are very likely to change the effect estimate.

Nerve Stimulation

Studies

Two studies were included which present findings in relation to the use of nerve stimulation devices designed to improve QOL amongst older stroke survivors [20,26]. Both studies were RCTs, conducted in specialist stroke or neurological rehabilitation units, with one conducted in the UK and the other in Sweden.

Participants

In total, 326 older adult stroke survivors participated in these trials, of which 179 (54.9%) were male. Table 4 presents a summary of participant characteristics for each of the nerve stimulation intervention studies.

Interventions

The two studies varied in their type of nerve stimulation, location of bodily impairment targeted and duration of treatment. Table 4 presents a summary of each interventions characteristics.

Risk of Bias

Both studies had a lack of or inadequate participant blinding procedures and are at risk of bias from small sample sizes. Insufficient reporting to clarify risk of several other bias sources resulted in a number of bias assessments being unclear.

Table 4 Participant Characteristics and Study Descriptions of Included Nerve Stimulation Interventions

Study	Arm	No. of Participants	Male/ Female	Age (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
Church 2006 [26]	I	176	89/ 87	75.5 (64-81) *	5 days (4-7) *	Surface neuromuscular electrical stimulation delivered over supraspinatus and posterior deltoid at 30hz.	One-hour session, 3 times per week	4 weeks
	C			73.5 (65-79) *		Sham treatment delivered as per intervention, but no electrical current delivered.	One-hour session, 3 times per week	4 weeks
Johansson 2001 [20]	I1	150	90/60	76 (9)	NR	Acupuncture treatment alternating between 2 modes (9 and 10 needlepoints) with low frequency electro stimulus.	Thirty-minute session, twice per week	10 weeks
	I2			77 (9)		Trans electrical nerve stimulation (TENS) treatment with high intensity low frequency electrodes used in same areas as acupuncture points.	Thirty-minute session, twice per week	10 weeks
	C			76 (11)		Sham treatment using the same equipment and electrode placement as TENS intervention, but with low intensity.	Thirty-minute session, twice per week	10 weeks

*Median and IQR given

C: Control I: Intervention I1: Intervention arm 1 I2: Intervention arm 2

Can the use of nerve stimulation devices effect older stroke survivors QOL scores in comparison to those who receive a sham treatment only?

Two studies [20, 26] explored the effectiveness of Transcutaneous Electrical Nerve Stimulation (TENS) upon older stroke survivors' QOL. Neither study could identify any significant differences between intervention or control groups at either 3 or 12 months post-intervention assessment (see table 5). The quality of the evidence was graded as very low and consequently there is no evidence to support a recommendation to use nerve stimulation techniques to improve QOL amongst older stroke survivors.

Table 5 Results of Studies Investigating the Impact of Nerve Stimulation Interventions Upon Older Stroke Survivors QOL

Study	Intervention	Control	p-value	GRADE Score	GRADE Comment
Church 2006 [26]	NHP (Median, IQR) 3mths: 31.2 (10.4-52.1)	NHP (Median, IQR) 3mths: 28.1 (15.7-48.2)	NHP 3mths p=ns	⊕◯◯◯ VERY LOW	a. Several sources of bias including unblinded patients b. Studies differ as one focuses on upper limb only while the other focuses on whole body, duration also differs (4weeks to 10 weeks). c. Small sample size
Johansson 2001 [20]	NHP (Median, IQR) *Acupuncture* 3 mths: 27 (16-39) 12 mths: 28 (8-42) *TENS* 3 mths: 30 (17-46) 12 mths: 34 (16-47)	NHP (Median, IQR) 3 mths: 34 (18-50) 12 mths: 32 (24-47)	NHP 3mths p=ns 12mths p=ns		

IQR: Interquartile Range NHP: Nottingham Health Profile Mths: Months NS: Not Significant

Occupational Therapy

Studies

Three studies were included and all were RCTs conducted in the UK [27-29].

Participants

A total of 681 older stroke survivors were recruited across the studies, of which 379 (55.7%) were male. Table 6 summarises participant characteristics from the included studies.

Interventions

Interventions varied widely in their content and duration and are summarised in table 6.

Risk of Bias

Unblinded or inadequately blinded participants represented the largest risk of bias arising from these studies.

Table 6 Participant Characteristics and Study Descriptions of included Occupational Therapy Interventions

Study	Arm	No. of Participants	Male/ Female	Age (Mean,SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
Parker 2001 [27]	I1	466	269/ 197	72 (65-79)*	NR	The treatment goals in the leisure group were set in terms of leisure activity and so interventions included practising the leisure tasks as well as any ADL tasks necessary to achieve the leisure objective.	Minimum of 10 sessions, each lasting at least 30 minutes	NR
	I2			71 (66-78)*		The treatment goals in the ADL group were in terms of improving independence in self-care tasks and therefore treatment involved practising these tasks (such as preparing a meal or walking outdoors).	Minimum of 10 sessions, each at least 30 mins.	NR
	C			72 (65-78)*		Usual care.	NR	NR
Walker 1996 [28]	I	30	16 / 14	65.9 (8.16)	NR	Treatment was given by a senior occupational therapist at the participants' home. Dressing practice was given on a regular basis, with the amount of therapy at the therapist's discretion. Treatment involved teaching participants and carers appropriate techniques such as dressing the effected limb first, energy conservation, the use of red thread to overcome perceptual difficulties and to mark alignment of buttons, and advice on choice of clothing. Relatives were encouraged to continue the dressing practice between sessions with the occupational therapist.	NR	3 months

	C			70.2 (10.35)		No intervention.	NR	3 months
Walker 1999 [29]		185	94/ 91	73.6 (8.1)	NR	Participants received visits from a research occupational therapist for up to 5 months. The frequency of treatment was agreed between the therapist, participant, and, if relevant, the carer. The aim of therapy was independence in personal and instrumental activities of daily living and the focus of therapy was active intervention rather than assessment or liaison.	Mean no. visits: 5·8 (SD 3·3) Mean length of each visit: 52 minutes (SD 11·8)	5 months
				75.1 (8.6)		No intervention	NR	NR

*Median and IQR given

C: Control I: Intervention I1: Intervention arm 1 I2: Intervention arm 2 IQR: Interquartile Range NR: Not Reported

What is the effectiveness of increasing OT intensity versus less/usual/ no OT upon older stroke survivors QOL scores?

Regarding the effect of total OT time on QOL, three trials reported relevant results (summarised in table 7). Walker *et. al.*, 1999 assessed the effectiveness of extra OT against no intervention, using the London Handicap Scale (LHS) as an outcome measure [29]. At six-month follow-up there was a small but statistically significant improvement favouring OT, with a mean difference of 6.75 points (95%CI [0.3; 13.5], p=0.03) [29]. Parker *et. al.* (2001) compared two OT techniques, leisure therapy and conventional ADL therapy, against no treatment [27]. They found no statistically significant differences between the intervention and control groups. An earlier study (Walker *et. al.*, 1996) which compared dressing-focused OT against no intervention reported a statistically significant difference of 4.62 between median changes in NHP scores, favouring the OT intervention (p=0.025) [28].

In view of the limited evidence, small number of studies, and inconsistency in findings, a GRADE quality assessment of low (see table 7) has been awarded. This review proposes that increased OT may be beneficial regarding QOL and so should therefore be available to older stroke survivors.

Table 7 Results of Studies Investigating the Impact of Increased Occupational Therapy Upon Older Stroke Survivors QOL Scores

Study	Intervention	Control	p-value	GRADE Score	GRADE Comment
Parker 2001 [27]	LHS (Mean, SD) *Leisure Therapy* 6mths: 64.5 (14.7) 12mths: 63.3 (16.3) *ADL Therapy* LHS (Mean, SD) 6mths: 62.7 (17.7) 12mths: 63.3 (18.2)	LHS (Mean, SD) *Control* 6mths: 63.5 (17.9) 12mths: 64.4 (18.8)	LHS All p=ns	⊕⊕◯◯ LOW	a. All 3 trials involved unblinded participants b. Two of the three interventions involved participants who had NOT been hospitalised due to their stroke, raising the possibility that these were less impaired than the hospitalised participants. c. One of three studies reported significant benefit favouring an increased OT intervention against usual care.
Walker 1996 [28]	NHP (Mean, SD) Base: 42 (17.3) 6mths: NR	NHP (Mean, SD) Base: 33.9 (5.4) 6mths: NR	NHP 6mths p=0.025		
Walker 1999 [29]	LHS (Median, IQR) 6mths: 76.1 (60.8-88.6)	LHS (Median, IQR) 6mths: 65.2 (47.9-86.9)	LHS Mean difference: 6.75 (0.3 to 13.5) p= 0.03		

Base: Baseline IQR: Inter-quartile Range LHS: London Handicap Scale Mths: Months NHP: Nottingham Health Profile NS: Not Significant SD: Standard Deviation

Physiotherapy

Studies

Eleven articles presenting nine studies presented findings in relation to PT interventions designed to improve QOL recovery of older stroke survivors [30-40]. All studies were randomised controlled trials, with two each conducted from Australia and the UK, and one each from the USA, Norway, Holland, Brazil and Sweden.

Participants

In total, 480 older stroke survivors participated in these trials, of which 248 were male (Duncan *et. al.,* 1998 [31] did not present participants sex information and so an overall % of male participants has not been calculated). A summary of participant characteristics is presented in table 8.

Interventions

The nine interventions varied widely regarding intervention content, delivery and duration, and each intervention is summarised in table 8.

Risk of Bias

Almost all studies were at risk of bias from unblinded or inadequately blinded participants. This said, most studies had adequate outcome assessor blinding. Several studies were at potential risk from biases resulting from randomisation or allocation methods.

Table 8 Participant Characteristics and Study Descriptions of included Physiotherapy Interventions

Study	Arm	No. of Participants	Male/ Female	Age Intervention Grp (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
Ada 2003 [30]	I	27	19/ 8	66 (11)	28 (17) months	Training sessions comprising of both treadmill and over ground walking.	30 to 45 minute sessions, 3 sessions per week.	4 weeks
	C			66(11)		A home exercise program consisting of exercises to lengthen and strengthen lower-limb muscles as well as to train balance and coordination.	3 sessions per week	4 weeks
Duncan 1998 [31]	I	20	NR	67.3 (9.6)	66 days (no SD)	Home based exercise program that included assistive and resistive exercises using Proprioceptive Neuromuscular Facilitation Patterns or Theraband exercises to the major muscle groups of the upper and lower extremities.	Three 90-minute sessions per week.	8 weeks
	C			67.8 (7.8)		Usual care and visited by a research assistant every 2 weeks to assess the participants' exercise and activity level.	Varied	8 weeks
GAPS 2004 [32]	I	70	41 / 29	68 (11)	NR	Additional physiotherapy input (aiming to approximately double the total daily physiotherapy time)	60 to 80-minute sessions, five sessions per week	Mean sessions per participant 43 (95% CI 35-51)

Study	Arm	No. of Participants	Male/ Female	Age Intervention Grp (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
	C			67 (10)		Usual physiotherapy input.	30 to 40-minute sessions, five sessions per week	Mean sessions per participant 32 (95% CI 24- 40)
Kwakkel 1999 [33] /2002 [34]	I1	101	43/ 58	69.0 (9.8)	7.2 (2.8) days	Additional arm training applied by local physical and occupational therapists and usual care (15 minutes per day leg rehabilitation, 15 minutes per day arm rehabilitation, and 90 minutes per week ADL training by an occupational therapist).	30 minutes per session, 5 sessions per week (and 4 hours per week usual rehabilitation)	20 weeks
	I2			64.5 (9.7)		Additional leg training applied by local physical and occupational therapists and usual care (15 minutes per day leg rehabilitation, 15 minutes per day arm rehabilitation, and 90 minutes per week ADL training by an occupational therapist).	30 minutes per session, 5 sessions per week (and 4 hours per week usual rehabilitation)	20 weeks
	C			64.1 (15.0)		Immobilisation of the paretic arm and leg by means of an inflatable pressure splint that was applied with the participant in supine position and usual care (15 minutes per day leg rehabilitation, 15 minutes per day arm rehabilitation, and 90 minutes per week ADL training by an occupational therapist).	30 minutes per session, 5 sessions per week (and 4 hours per week usual rehabilitation)	20 weeks
	I	61	36 / 25	NR	NR	Motor relearning (no further detail given).	NR	NR

Study	Arm	No. of Participants	Male/ Female	Age Intervention Grp (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
Langhammer 2000 [35] /2003 [36]	C			NR		Bobath (no further details)	NR	NR
McClellan 2004 [37]	I	26	13 / 13	69 (13)	6.5 (5.5) months	Exercises were aimed at improving mobility in standing and walking. Intervention was standardised by prescribing the first five exercises that the subject could not perform successfully from a list of 23 predetermined exercises. Each subject attended a local physiotherapy department for the initial prescription of exercises and the exercises were recorded on videotape. Subjects were instructed to practise each exercise twice a day in front of the videotape. Participants returned to their outpatient department to have their exercises reviewed and progressed at Weeks 2 and 4	2 sessions per day	6 weeks

Study	Arm	No. of Participants	Male/ Female	Age Intervention Grp (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
	C			72 (9)		The exercises prescribed for the control group were aimed at improving the function of the effected upper limb. The intervention was standardised by prescribing the first five exercises that the subject could not perform successfully from a list of 39 predetermined exercises. Each subject attended a local physiotherapy outpatient department for the initial prescription of exercises and the exercises were recorded on videotape. Subjects were instructed to practise each exercise twice a day in front of the videotape. Participants returned to their local physiotherapy outpatient department to have their exercises reviewed and progressed at Weeks 2 and 4.	2 sessions per day	6 weeks
Morris 2008 [38]	I	106	61/55	67.9 (13.1)	22.6 (5.6) days	Participants practice 4 different tasks (up to 30 practices per task, per session) with both arms, simultaneously.	20 minutes per day, 5 days per week	6 weeks
	C			76.8 (9.9)		As per intervention but are performed with only the paretic arm.	20 minutes per day, 5 days per week	6 weeks
Sandberg 2016 [39]	I	29	14/15	71.3 (7.0)	Median of 20 days (no IQR reported)	Group high intensity aerobic exercise sessions led by a PT and intensity measured by heart rate monitors.	Two 60-minute sessions per week	12 weeks
	C	27	14/13	70.4 (8.1)		Usual care.	NR	NR

Study	Arm	No. of Participants	Male/ Female	Age Intervention Grp (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
Teixera-Salmela 1999 [40]	I	13	7 / 6	65.87 (10.16)	9.15 (12.72) years	Supervised exercise sessions held by exercise physiologist and PT. Includes warm up, aerobic exercises, strength training and cool down.	60 to 90-minute sessions, 3 sessions per week	10 Weeks
	C			69.42 (8.85)		No intervention.	NR	NR

*Median and IQR given

C: Control I: Intervention I1: Intervention arm 1 I2: Intervention arm 2 NR: Not Reported PT: Physiotherapist Sev.: Severe SD: Standard Deviation

What is the effectiveness of increased intensity PT or additional PT versus versus usual/standard amount of PT or no PT upon older stroke survivors QOL scores?

Regarding the effect of total PT time on QOL outcomes, five studies reported relevant results (see table 9 for summary of results). Duncan *et.al*. (1998) found no statistically significant differences in SF36 scores between those who received an eight-week intensive home exercise programme and those receiving usual care [31]. Kwakkel *et.al.* (1999) compared SIP and NHP scores between those receiving intensive arm training, intensive leg training or usual care. SIP scores at the three-month follow-up were significantly different, favouring leg training ($p<0.05$).However, no significant differences from six-month follow-up onwards were identified [33]. Similarly, Sandberg *et.al.* (2016) found that immediately following the intervention (12 weeks) intervention participants QOL had significantly improved versus those in the usual care control group ($p<.006$) [39].However, no significant differences in the long term could be identified. GAPS (2004) reported that their intervention participants, who received double the duration of physiotherapy than control participants, had significantly higher QOL scores at 6 months than their control counterparts ($p=0.009$) [32]. Teixeira *et.al*. (1999) also reported significant improvements in QOL at the end of a 10-week exercise programme favouring the intervention ($p=.008$) [40]. However, no long-term post-intervention follow-up was reported to indicate longevity of such an improvement.

Across the five studies, the results are conflicting. The GRADE assessment suggests the quality of the evidence base is low (see table 9). In view of the limited evidence, this review proposes that increased PT may be beneficial regarding QOL and so should therefore be available to older stroke survivors but further research is required to examine this relationship further.

584 **Table 9 Results of Studies Investigating the Impact of Additional Physiotherapy Interventions Upon Older Stroke Survivors Quality of Life**

Study	Intervention	Control	p-value	GRADE Score	GRADE Comment
Duncan 1998 [31]	MoS36 (Mean, no SD reported) Base: 28.5 8wks: 44.0 Change: 15.5	MoS36 (Mean, no SD reported) Base: 35.5 8wks: 44.5 Change: 9	MoS36 Difference between change: p= >0.2	⊕⊕◯◯ LOW	a. All four studies had unblinded participants and one study had almost all unclear risks of bias due to lack of information provided. b. Results were inconsistent, with two studies reporting quite significant improvement on QOL scores while two found no significant difference in scores. c. Four different measures of QOL were utilised across the four studies, and only 2 of the 4 studies reported significant results favouring PT intervention against usual care control participants.
GAPS 2004 [32]	EuroQOL (Mean, SD Base: 53.7 (18.2) 6mths: 62.3 (24.6) Change: 9.78 (30.8)	EuroQOL (Mean, SD) Base: 52.4 (18.9) 6mths: 51.8 (23.5) Change: -2.0 (20.8)	Mean difference: 6mths: -10.5 (-22.8, 1.8) p=0.09 Difference between change: -11.7 (-26.3, 2.8) p= 0.11		
Kwakkel 1999 [33]	*Arm Training* SIS (Mean, SD) Base: NR 12wks: 31.1 (11.4) 26wks: 27.9 (13.1) NHP (Mean, SD) Base: NR 12wks: 10.4 (7.3) 26wks: 9.5 (5.9) *Leg Training* SIS (Mean, SD) Base: NR 12wks: 26.9 (12.5) 26wks: 25.7 (12.7)	*Control* SIS (Mean, SD) Base: NR 12wks: 36.8 (11.7) 26wks: 32.9 (12.0) NHP (Mean, SD) Base: NR 12wks: 14.5 (5.6) 26wks: 11.6 (7.9)	SIS 12wks: mean difference between Arm and Leg : p<0.05. All other p=ns NHP all p=ns		

Study	Intervention	Control	p-value	GRADE Score	GRADE Comment
	NHP (Mean, SD) Base: NR 12wks: 9.4 (6.1) 26wks: 9.8 (8.1)				
Sandberg 2016 [39]	EQ5D Index (Mean, SD) Base: .75 (.16) 12wks: .85 (.12) Change: .10 (.16) 6mths: .88 (.12) Change: .03 (.17) EQ5D VAS (Mean, SD) Base:72.3 (22.3) 12wks: 87.2 (9.1) Change: 15.0 (19.2) 6mths: 89.6 (11.2) Change: 2.3 (7.9)	EQ5D Index (Mean, SD) Base: .81 (.21) 12wks: .78 (.31) Change: -.03 (.33) 6mths: .82 (.27) Change: .03 (.22) EQ5D VAS (Mean, SD) Base:80.4 (18.9) 12wks:81.1 (17.5) Change: .7 (17.7) 6mths: 84.7 (18.3) Change: 3.5 (16.2)	EQ5D Index Base: .221 12wks: .344 Cahnge: NR 6mths: .344 Change: NR EQ5D VAS Base: .185 12wks: .159 Change: <.006 6mths: .291 Change: NR		
Teixera 1999 [40]	NHP Base: 9.33 (8.24) 10wks: 1.17 (1.47)	NHP Base: 11.14 (4.10) 10wks: 10.14 (4.98)	NHP Base: NR 10 wks p=.008.		

Base: Baseline Euro QOL: European Quality of Life MOS36: Medical Outcomes Study 36 Mths: Months NHP: Nottingham Health Profile NR: Not Reported
NS: Not Significant SIS: Stroke Impact Scale Wks: Weeks

What is the effectiveness of specific PT approaches versus alternative PT approaches or usual care upon older stroke survivors QOL recovery?

Regarding the effectiveness of different types of PT, five studies reported relevant results which are summarised in table 10. Of these five studies, none demonstrated any significant benefit upon participants QOL scores post intervention. A quality assessment, using the GRADE approach, assesses the quality of this evidence as being very low (see table 10), suggesting that further studies are very likely to change this. The variance in intervention content and design, with unblinded participants and a small overall sample size, contributed towards this. Therefore, it is not possible for this review to make any recommendations regarding the use of specific PT approaches in place of alternative approaches to enhance QOL.

Table 10 Results of Studies Investigating the Impact of Alternative Physiotherapy Interventions Upon Older Stroke Survivors Quality of Life

Study	Intervention	Control	p-value	GRADE Score	GRADE Comment
Ada 2003 [30]	SIP (Mean, SD) Base: 12.1 (5.5) 1mth: 12.0 (6.5) 3mths: 9.8 (6.0)	SIP (Mean, SD) Base: 15.2 (5.2) 1mth: 13.6 (6.1) 3mths: 13.2 (5.4)	SIP 1mth: p=0.85 3mths: p=0.69	⊕◯◯◯ VERY LOW	a. All studies had unblinded participants and several unclear sources of bias risk. b. All trials compared different types of PT and therefore content and delivery varied widely. c. Small overall sample size
Langhammer 2000 [35] /2003 [36]	NHP (Mean, SD) 3mths: 22 (18) 12 mths: 17 (16) 48 mths: 20 (15)	NHP (Mean, SD) 3 mths: 24 (21) 12 mths: 13 (12) 48 mths: 16 (11)	NHP All p=ns		
McClellan 2004 [37]	SIP (Mean, SD) Base: 16.5 (6.1) 6wks: 15.5 (6.2) 14wks: 14.2 (7)	SIP (Mean, SD) Base: 12.6 (5.9) 6wks: 11 (5.7) 14wks: 11.5 (6.3)	SIP 6wks: p=0.70 14wks: p=0.60		
Morris 2008 [38]	NHP (Mean, SD) Base: 180 (121) 6wks: 126 (101) 18wks: 122 (110)	NHP (Mean, SD) Base: 174 (118) 6wks: 104 (85) 18wks: 92 (92)	NHP Base: p=NR 6wks: p=0.25 18wks: p=0.34		

Study	Intervention	Control	p-value	GRADE Score	GRADE Comment
Kwakkel 1999 [33] / 2002 [34]	SIS Arm Training (Mean, SD) 12 wks: 31.1 (11.4) 26 wks: 27.9 (13.1) NHP 12 wks: 10.4 (7.3) 26 wks: 9.5 (5.9) SIS Leg Training (Mean, SD) 12 wks: 26.9 (12.5) 26 wks: 25.7 (12.7) NHP 12 wks: 9.4 (6.1) 26 wks: 9.8 (8.1)	SIS Control (Mean, SD) 12 wks: 36.8 (11.7) 26 wks: 32.9 (12.0) NHP 12 wks: 14.5 (5.6) 26 wks: 11.6 (7.9)	SIS All p=ns NHP All p=ns		

Base: Baseline 2 Mths: Months NHP: Nottingham Health Profile NR: Not Reported NS: Not Significant SD: Standard Deviation SIP: Sickness Impact Profile SIS: Stroke Impact Scale Wks: Weeks

Self-management Education

Studies

Five studies were included in this review that present findings in relation to self-management education interventions designed to improve older stroke survivors QOL [41-45]. All studies were RCTs, with two conducted in Australia, two in Canada and one in the UK.

Participants

In total, 485 older stroke survivors participated in these trials, of which 245 (50.5%) were male. A summary of participant characteristics is presented in table 11.

Interventions

While each of the five interventions focused upon providing post-stroke education and developing self-management skills and plans, their content and mode of delivery varied, as described in table 11.

Risk of Bias

Each of the five studies had at least one significant risk of bias, most usually arising from unblinded or inadequately blinded participants. Several studies also were at high risk of bias arising from their randomisation and allocation methods.

Table 11 Participant Characteristics and Study Descriptions of included Self-management Education Interventions

Study	Arm	No. of Participants	Male/ Female	Age (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
Cadilhac 2011 [41]	I1	143	59/84	NR	NR	Stroke specific group self-management programme built upon generic Stanford model but includes only stroke survivors and more contact time.	2.5 hour session once per week	8 weeks
	I2			NR		Generic Stanford group self-management programme, where no more than one third of participants had stroke, to ensure the programme was realistic of generic programmes involving persons with wide range of conditions.	2.5 hour session once per week	6 weeks
	C			NR All= 69.4 (11.45)		Usual care.	NR	NR
Desrosiers 2007 [42]	I	62	30/ 32	NR	NR	12-step programme delivered by recreational therapist and overseen by an occupational therapist, to optimise leisure activity engagement.	One hour weekly sessions.	8-12 weeks
	C			NR *All=70.8 (10.8)*		Sham intervention involving social visits from the therapist.	One hour weekly sessions.	8-12 weeks
Forster & Young 1996 [43]	I	240	127/ 113	73 (60-94) *	NR	Programme of home visits conducted by specialist nurses. Participants were provided stroke information and encouraged to identify problems and solutions, to set goals, and return to social activities.	Minimum 6 visits in first 6 months.	Up to 12 months.
	C			73 (60-90) *		Usual care.	NR	NR

Study	Arm	No. of Participants	Male/ Female	Age (Mean, SD)	Time post-stroke (Mean, SD)	Description	Timing	Treatment Length
Nour 2002 [44]	I	14	10 / 4	71.1 (9.5)	NR	A 12-step individualised programme aiming to encourage participant to self-manage their leisure activities.	One hour session per week	10 weeks
	C			71.7 (8.7)		A flexible social programme involving weekly sessions with therapist to discuss different topics such as family, news etc.	One hour session per week	10 weeks
Marsden 2010 [45]	I	26	19 / 7	70 (9)	37.2 months (26.7)	CLASSIC, Community Living After Stroke for Survivors and Carers programme, was delivered in a small group setting and exercise and education sessions, plus a short tea break where healthy eating, encouragement to engage in conversation, and encouragement to use effected limbs, was attempted.	2.5-hour session per week	7 weeks
	C			73.1 (9.3)		Usual care.	NR	NR
	C			76 (36-95)*		Usual care.	NR	NR

*Median and IQR given

C: Control I: Intervention I1: Intervention arm 1 I2: Intervention arm 2 NR: Not Reported OT: Occupational Therapy PT: Physiotherapy SD: Standard Deviation

Do self-management education interventions effect post-stroke quality of life scores of older stroke survivors in comparison to those who receive usual rehabilitation care?

Five studies explored the impact of self-management education interventions upon post-stroke QOL of older stroke survivors (results summarised in table 12). Of these, only one study, Nour *et. al.* (2002), identified a significant difference in post-intervention QOL scores [44]. This small pilot study (n=14) of a 12-week leisure education programme found that the intervention group mean SIP 30 scores increased from 20.4 (2.7) to 26.2 (2.2). However, control participants had a slight decrease in SIP 30 scores, from 19.1 (3.4) to 18.4 (2.6). Between group differences were highly significant, favouring the intervention group (p= .008) [44]. However, this study was unable to replicate its results in a full and larger trial of the same programme (n=62), later published by Desrosiers et al (2007) [42]. The limited evidence does not support the use of self-management education interventions to improve older stroke survivors QOL. The one small study which demonstrated significant improvement was unable to replicate this result in a later, and larger, trial. A quality assessment of the included studies, using GRADE approach, rated the evidence as low (see table 12), meaning that further studies are likely to change the expected outcome from the findings of these five trials.

Table 12 Results of Studies Investigating the Impact of Self-management Education Interventions Upon Older Stroke Survivors Quality of Life

Study	Intervention	Control	p-value	GRADE Score	GRADE Comment
Cadilhac 2011 [41]	*SSMP* AQOL (Mean, SD) Base: NR 6mths: 0.0008 (0.03) *Generic Programme* AQOL (Mean, SD) Base: NR 6mths: -0.02 (0.02)	*Control* AQOL (Mean, SD) Base: NR 6mths: 0.02 (-0.03)	AQOL (Scale range -.0.04 to 1= good health) control v generic p=0.61 control v SSMP p=0.90	⊕⊕◯◯ LOW	a. 2 studies reported unblinded participants while the others were unclear regarding several methodological aspects including blinding, randomisation and allocation concealment. b. Substantial variation in delivery, content and duration of interventions c. Studies utilised a variety of measures for QOL, and only one of the five studies reported a significant result favouring the self-management intervention.
Marsden 2010 [44]	SIS QOL (Mean, SD) Base: 82.3 (17) 9wks: 84.9 (13.2) 21wks: 84.4 (15.7)	SISQOL (Mean, SD) Base: 82.2 (19.1) 9wks: 84.4 (23) 21wks: 84.5 (18.4)	SISQOL All between group differences p=ns		
Nour 2002 [44]	SIP30 (Mean, SD) Base: 20.4 (2.7) Post-test: 26.2 (2.2) -	SIP30 (Mean, SD) Base: 19.1 (3.4) Post-test: 18.4 (2.6)	SIP30 Baseline p=0.54 Post-test p=0.01 Mann Whitney test for change over time between 2 groups p=0.008		
Desrosiers 2007 [42]	SIP30 (Mean, SD) Base: 8.1 (3.6) Post-test: 6.9 (3.4) -	SIP30 (Mean, SD) Base: 11.6 (4.6) Post-test: 10.1 (3.9)	SIP30 Between group difference over time= 0.2 (-1.3, 1.8) p=0.76.		

Study	Intervention	Control	p-value	GRADE Score	GRADE Comment
Forster & Young 1996 [43]	NHP (Median, IQR) Base: 93 (38-152) 3mths: 96 (24-171) 6mths: 96 (125-169) 12mths: 97 (24-184)	NHP (Median, IQR) Base: 70 (24-181) 3mths: 78 (24-196) 6mths: 84 (29-175) 12mths: 80 (26-172)	All between group differences p=ns		

643 AQOL: Assessment of Quality of Life NHP: Nottingham Health Profile NR: Not Reported NS: Not Significant SIP30: Sickness Impact Scale 30 SISQOL: Stroke

644 Impact Scale Quality of Life SSMP: Stroke Self-management Programme

Video Games

Studies

One study investigated the role of videogames in the treatment of older stroke survivors. The RCT was conducted in the UK [46].

Participants

The trial by Adie (2017) involved 235 participants, 131 (55.7%) of whom were male [46].

Interventions

Participants were taught and encouraged to play sport games (e.g. bowling, tennis, golf and baseball) using a Nintendo Wii device [46]. Participants were asked to play these games for up to 45 minutes per day, each day, for six weeks [46]. Control participants were provided individually tailored arm exercises for a similar amount of time as intervention participants were asked to engage in game training [46].

Risk of Bias

The study is generally of low bias risk, however adequacy checks on assessor blinding suggest blinded assessment may not have been as effective as planned

Can arm exercises delivered via video games benefit stroke survivors QOL more than arm training exercises without video game component?

Adie (2017) investigated whether use of the Nintendo Wii Sports Games could benefit stroke survivors QOL more so than standard prescribed arm exercises [46]. No significant differences between the groups SIS or EQ5D scores were identified at either six weeks (end of intervention) or at six months [46]. As a result of one study (n=235), which demonstrated no improvement in QOL, we are unable to recommend the use of videogames to improve QOL amongst older stroke survivors. Using the GRADE system, the results suggest the evidence is of low quality, meaning that further studies are very likely to change results

Recommendations

Table 13 presents a summary of the recommendations this study can make based on the evidence identified from this systematic review.

Table 13 Summary of Recommendations for Each Category of Non-pharmacological Intervention

Category	Recommendation
Acupuncture	There is no evidence to show that acupuncture can benefit older stroke survivors QOL and GRADE assessment of this evidence suggests the quality is low. Therefore we cannot recommend acupuncture for older stroke survivors.
Caregiver Training	There was limited evidence to show that caregiver training can benefit older stroke survivors QOL. Only one study was considered in this category and was given a GRADE quality assessment score of low. Therefore, we are unable to recommend caregiver training to benefit older stroke survivors QOL.
CIMT	Evidence from one study showed that CIMT can improve older stroke survivors QOL. However, the evidence from one study was assessed by GRADE to be of low quality. Therefore, we cannot recommend the use of CIMT for older stroke survivors.
Device assisted Physiotherapy	There is very limited evidence to support the use of device-assisted physiotherapy to enhance older stroke survivors QOL, and the evidence was given a GRADE quality assessment score of low. Therefore, we cannot recommend device assisted physiotherapy for older stroke survivors
Music Therapy	There is no evidence to show that music therapy can benefit older stroke survivors QOL and GRADE assessment of this evidence suggests the quality is low. Therefore we cannot recommend music therapy for older stroke survivors.
Nerve Stimulation	There was no evidence that nerve stimulation can benefit older stroke survivors QOL. The quality assessment score was very low. Therefore, we cannot recommend nerve stimulation to benefit older stroke survivors ADL

Category	Recommendation
Occupational Therapy	There is limited evidence to show that additional occupational therapy can benefit older stroke survivors QOL. GRADE quality assessment suggests the quality of the evidence to be low. Therefore, the use of additional occupational therapy can be recommended as it may benefit older stroke survivors.
Physiotherapy	There is some evidence to show that additional physiotherapy can benefit older stroke survivors QOL. The GRADE quality assessment score was low. Therefore, the use of additional physiotherapy can be recommended as it may benefit older stroke survivors QOL.
Self-management Education	There is very limited evidence to show that self-management education programmes can benefit older stroke survivors QOL, and the GRADE quality assessment score was low. Therefore we cannot recommend self-management education programmes to benefit older stroke survivors.
Video Games	There is no evidence to show that videogames can benefit older stroke survivors QOL and GRADE assessment of this evidence is moderate. Therefore we are unable to recommend videogame intervention to benefit older stroke survivors.

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Discussion

Acupuncture

Across the guidelines, there is little mention of acupuncture as a therapy for stroke survivors. RCP (2016) refer to the limited evidence for acupuncture in the treatment of dysphagia [3], and SIGN (2010) state that they do not recommend acupuncture for the treatment of post-stroke pain syndromes due to insufficient evidence [4]. Teasel et al (2003) in a discussion regarding interventions to promote ADL post-stroke state that the evidence for acupuncture is conflicting [47]. Within the present review, there was no evidence to show that acupuncture can benefit older stroke QOL.

Caregiver Training

RCP (2016) stroke guidelines acknowledges the insufficient evidence behind the benefits of caregiver training as part of stroke rehabilitation [3]. The guidelines do however note that the involvement of carers at all stages of rehabilitation is important and considered good practice [3-4]. In our review of interventions exclusive to older stroke survivors, only one study exploring the impact of caregiver training upon patient QOL was identified [22]. This study was sufficiently large, and demonstrated consistent improvement in participant QOL. Therefore, caregiver training may be beneficial, but further high quality research is required to examine this intervention further.

CIMT

Evidence from one study showed that CIMT could improve QOL scores [23]. However, the quality of the evidence for this was weak. Veerbeek et al (2014) found little evidence to support the use of CIMT

to improve QOL of adult stroke survivors; while there was a significant benefit upon ADL scores following low intensity modified CIMT, this type of intervention had no significant impact upon QOL [48]. Original and high intensity CIMT demonstrated no benefit upon ADL or QOL [48]. In view of the evidence, SIGN (2010) specifically state that *"Constraint induced movement therapy may be considered for carefully selected individuals with at least 10 degrees of finger extension, intact balance and cognition"* (p20) [4]. RCP (2016) also report that benefits of CIMT often relate only to arm function and within the confines of the activities used within the intervention [3]. Evidence from both the general adult population of stroke survivors, and in the context of older stroke survivors, appears limited in relation to QOL. As is similar to other stroke rehabilitation interventions, CIMT appears most effective when effectiveness is measured in terms of its immediate effect, but these benefits do not appear to be associated with improvements in more comprehensive outcomes.

Device assisted PT

There was limited evidence to support the use of device assisted PT to enhance older stroke survivors QOL. Our findings are similar to those found by Veerbeek et al (2014) who found no significant benefit in relation to QOL from device assisted PT techniques such as robotic assisted arm training and trunk restraint training in their review of PT interventions amongst stroke survivors [48]. The use of robotic devices has been recommended by Teasel et al (2003) as they considered this approach beneficial for those with impaired arm function, but this recommendation was based on achieving improved arm function, not global outcomes such as QOL [47]. Conversely, because of the overall low quality of evidence behind robot assisted movement therapies the RCP (2016) guidelines stipulate that this type of therapy should only be offered as an adjunct to conventional therapy and within the context of a clinical trial [3].

Music Therapy

Only one study explored music therapy specifically in relation to older stroke survivors QOL, and no evidence was presented suggesting the intervention could benefit this outcome [25]. Music therapy has been explored previously within neuro-rehabilitation and reviews have identified several benefits such as improved motor function, language and mood [49-51]. Nevertheless, their efficacy within older stroke survivors remains unknown.

Nerve Stimulation

We identified and reviewed two studies exploring the efficacy of nerve stimulation devices to improve older stroke survivors' QOL [20, 26]. Evidence to date has shown that while nerve stimulation techniques can improve specific impairments, such as muscle strength or gait, these improvements do not lead to significant improvements in global measures [3]. Within this analysis, no evidence was identified to support a role for nerve stimulation to improve QOL. The number of studies focusing exclusively upon older stroke survivors is small, making it difficult to sub-divide studies into those focusing on specific types of stimulation or use of stimulation in different locations (e.g. upper or lower body). Larger reviews, which have included adult participants of all ages, suggest the best evidence may be found in the use of nerve stimulation for upper limb impairments [48, 52]. Overall the evidence has many inconsistencies and remains insufficient to make any recommendations [4].

Occupational Therapy

There was limited evidence to show that additional OT may benefit older stroke survivors' quality of life, consistent with the findings of another similar systematic review [53]. Our

review also found no evidence to support that one OT approach above another is beneficial to older stroke survivors QOL, consistent with the review by Teasel *et. al*. (2003) [47]. All guidelines recommend OT, which focuses upon ADL, as an important feature of stroke rehabilitation, but acknowledge that the intensity and duration which provides best benefits is yet to be determined [3-4]. The relationship between ADL and QOL amongst stroke survivors is complex, but it has been suggested that early improvements in ADL contributes towards improved QOL in the longer term [54].

Physiotherapy

There was some evidence to show that additional PT can benefit older stroke survivors' QOL. It has been reported that many interventions which fall under PT such as balance exercises, gait training, and fitness training do lead to benefits in their respective objectives i.e. improved balance, gait, cardiovascular fitness [47]. However, similar to nerve stimulation, these benefits are rarely associated with improvement in more global measures [47-48]. In relation to QOL, combined strength and cardiovascular exercises, and high intensity practice, both demonstrate positive benefit upon stroke survivors QOL [48]. In this present review, the resulting number of included studies is considerably smaller than cited in reviews such as that the review by Veerbeek *et. al.* (2014) [48]. This is likely due to our focus on older adults and global outcomes. Nevertheless, we found some evidence of benefit in an older population with stroke of higher intensity physiotherapy input compared to standard or no input.

Self-management Education

Current guidelines suggest self-management to be capable of influencing function and social participation, able to address unmet patient needs, and so should be offered to stroke survivors [3]. In relation to QOL, this review identified limited evidence to suggest that self-management education programmes can benefit older stroke survivors' QOL. A previous systematic review of self-management interventions for stroke survivors reports that such interventions can benefit several psycho-social outcomes [55]. However, the only study presenting evidence for QOL in their review, a study by Kendall et.al., 2007 [56] reported single domains of a global QOL measure (family roles and fine motor tasks), and not a global QOL score as was sought by the present review. A recent qualitative exploration of stroke survivors feelings towards self-management suggest there is patient support for such interventions to address feelings of helplessness and abandonment post-stroke discharge, but disagreement between patients as to how best this can be provided, with patients keen that such support be individualised [57]. Therefore, further work is required to understand how such interventions can better improve psycho-social outcomes such as QOL.

Video Games

Current guidelines report that the evidence behind videogames as a stroke rehabilitation approach is weak to moderate [3-4]. A Cochrane review by Laver *et. al.* (2015) investigating the role of such interventions in stroke recovery, suggests that videogames can benefit stroke survivors, but that evidence is limited to younger stroke survivors and those who are more than one-year post-stroke [58]. This review identified only one study which explored the impact of videogames upon older stroke survivors QOL and this study was unable to demonstrate any benefit. However, evidence identified by studies involving younger stroke survivors [58] suggests further research of this intervention type amongst older stroke survivors is warranted.

Limitations

As with all studies, this review has several limitations that must be considered alongside our findings. Firstly, we did not involve patients or carers in the Delphi process. Therefore our identified critical outcomes may not reflect the preferences of patients and their carers. Due to the heterogeneity between studies, this review has largely been limited to narrative analysis only. While describing comparisons between studies is important, it has potential for researcher bias through the imposition of the researchers own subjective ideas about the findings and lacks the rigour of qualitative and objective analysis. As several reviewers were involved in the data extraction and analysis this does reduce this risk however we cannot rule out the potential for researcher bias. Although we used the GRADE criteria recommended by the Cochrane Collaboration this also introduced a degree of subjectivity. This means our results should be interpreted cautiously. We also cannot exclude the possibility that this review has omitted important studies. We have not searched the grey literature and our search strategy focused exclusively on identifying systematic reviews which may have resulted in omission of some trials, particularly those more recently published. However, our comprehensive strategy and the checking of reference lists and published clinical guidelines does go some way in reducing this risk. Categories of non-pharmacological interventions were developed through discussions between the researchers and we acknowledge these are somewhat arbitrary. For example, it could be argued that interventions exploring nerve stimulation devices, which are often delivered by trained physiotherapists, could be considered an alternative PT approach, as opposed to a category in its own right. Our decisions regarding categorising interventions were largely pragmatic and aimed to organise and present findings in a meaningful way. However, findings should be interpreted with caution since the interventions lack specificity. In our recommendations, we also do not consider the preferences of patients and their carers regarding intervention types. Little work has been done on this area within older stroke survivors and it is not known how acceptable different non-pharmacological approaches to stroke rehabilitation are to patients.

The principal difficulty we experienced, and limits the recommendations we can make, is the significant lack of published studies that met our age criteria (mean age≥ 65 years) and present data regarding our critical outcome, QOL. In relation to age, most studies reported sample groups with mean ages around 70 years and therefore our findings our not necessarily representative of the oldest old (e.g. ≥ 80 years). In relation to outcome, whilst we believe it was right to focus upon expert consensus opinion regarding important outcomes of non-pharmacological interventions for stroke rehabilitation, we excluded a number of papers (n=35) as a consequence. These papers often reported more specific measures in relation to the impairment the intervention targeted, such as improved gait, balance or muscle strength, and few specifically targeted QOL. This likely explains the absence of certain categories of interventions. For example, there were no systematic reviews or primary studies involving speech therapy due to these studies not reporting our required outcomes, instead focusing upon outcomes directly related to the therapy itself e.g. reducing symptoms of aphasia or dyspraxia. These therapies may have proven beneficial if QOL had been reported. Another important finding was that QOL was almost always a secondary outcome, suggesting that many therapies and their studies are not being designed from a QOL perspective. A substantial number of papers were excluded following review of title and abstract based on age (n=107). While this is a clear example of age discrimination in research [59], the use of age-based criteria in our work is arguably a strength. It allows us to examine the evidence as it specifically relates to older adults, but it risks excluding interventions that may be beneficial but have not been investigated in an older population. The impact of age as a modifier of treatment effect for many of the interventions examined is unknown.

Additionally, this review uncovered a number of methodological and reporting problems, making the ascertainment of the evidence challenging, such as the diverse range of QOL measures. No agreed standards for assessing stroke survivors QOL have been identified and each measure assesses quite

different domains, making comparisons difficult. Small sample sizes and failure to adequately report details regarding participant selection, randomisation, allocation concealment and data analysis, especially the management of missing data, led to many studies being deemed high risk of bias. Varied, limited and inconsistent descriptions of participant characteristics regarding stroke severity and stroke related disability between studies makes heterogeneity difficult to assess. One important challenge regarding RCTs involving non-pharmacological treatments is the lack of participant blinding. Although blinding of non-pharmacological treatments is challenging, reviews do highlight many creative approaches to doing so [60]. However, opinions regarding the importance of this are divided. Lack of patient blinding in RCTs presents opportunity for bias, particularly for subjective outcomes [60] such as those explored in the present manuscript. However, concerns have been raised about false negative results arising from RCTs involving non-pharmacological treatments as a result of blinded participants [61]. It is argued that what factors blinding controls for may be an integral component of non-pharmacological therapy [61]. For example, the additional care an intervention participant may receive as part of their acupuncture treatment may contribute towards overall benefit of the treatment [61]. In pharmacological RCTs this additional care would be considered incidental and would be controlled for through provision of similar care to control participants [60-61]. However, it has been argued that this takes away from some of the benefits non-pharmacological treatments bring, and therefore leads to findings of no-benefit [61]. It may be prudent for future work to explore the role of incidental and placebo effects in non-pharmacological treatments for stroke survivors to enhance our confidence in future results.

To surmise, further work exploring the impact of non-pharmacological interventions upon stroke survivors QOL is necessary. Specifically, trials which have been designed with the primary aim of improving QOL will be most beneficial to understanding the efficacy such interventions. Several such trials, mostly surrounding self-management and behavioural interventions, and designed specifically

to target QOL, have recently been registered [62-64]. The results of which will help to clarify our understanding of their efficacy and progress our knowledge regarding an important but under-researched outcome in stroke rehabilitation.

Conclusion

Limited evidence suggests additional or alternative approaches of PT or OT may benefit older stroke survivors QOL against usual PT or OT delivered as usual or standard care (as per current national and international stroke management advice). Limited evidence also suggests caregiver training, self-management education, device assisted physiotherapy, and CIMT may benefit older stroke survivors QOL against no such intervention.

However, current evidence is limited by low to very low quality and therefore recommendations for these approaches are based on weak evidence. This review revealed a distinct lack of evidence for the use of non-pharmacological interventions for stroke survivors aged 65 years and older. Of studies that did involve those aged 65 and older, evidence is limited by poor study designs and inadequate study reporting. Therefore, in addition to our recommendations regarding non-pharmacological approaches to treat older stroke survivors, we also recommend that future studies explore these interventions exclusively in older adult populations and ensure studies are adequately reported both in terms of methodological detail but also in terms of their outcomes.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Supporting Information

Fig. 1 ONTOP Review Methodology.tiff

Fig. 2 Study Selection Process.tiff

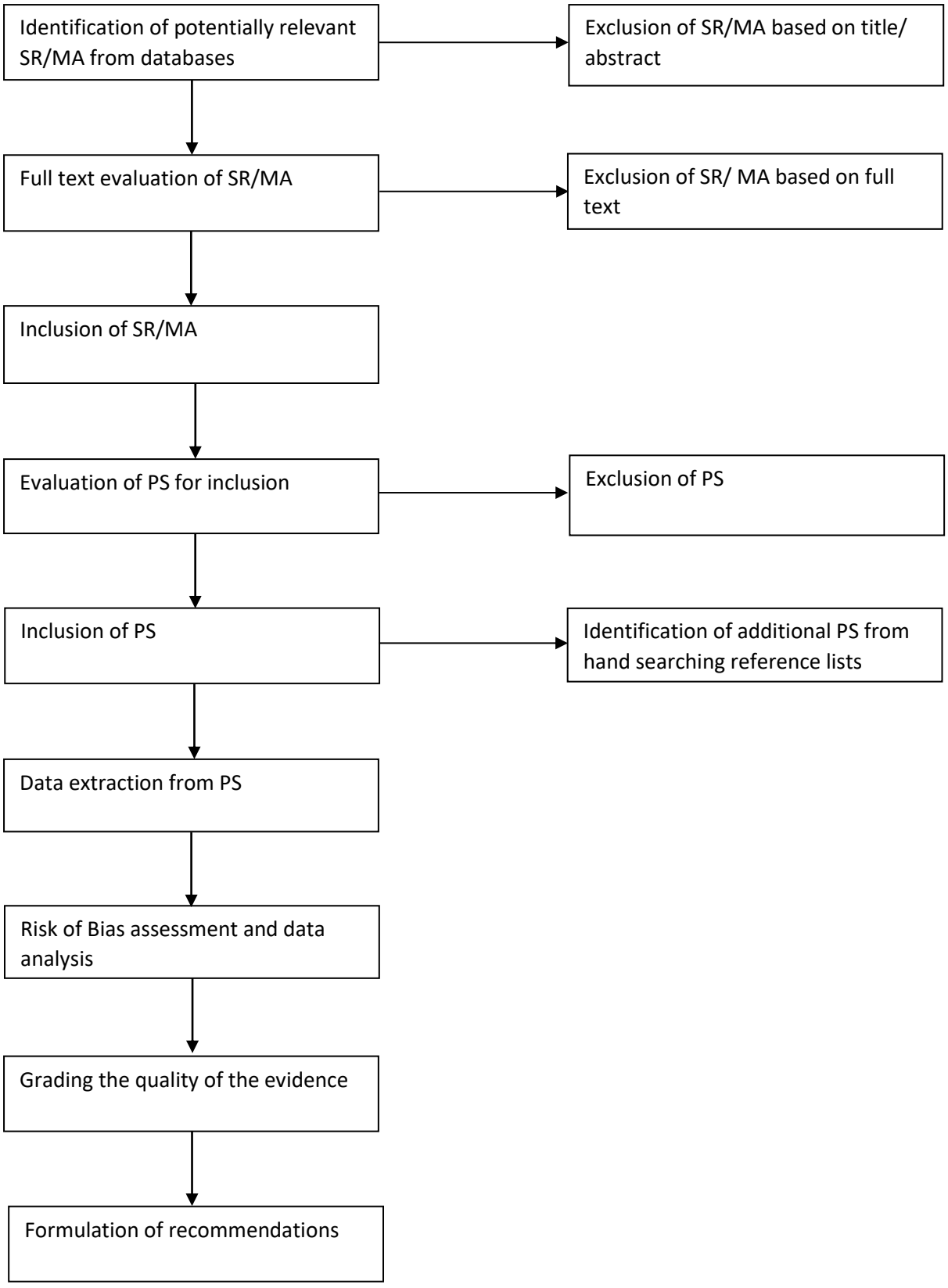
Online Resource 1 PRISMA Checklist.pdf

Online Resource 2 Database Search Strategies.pdf

Online Resource 3 References of Studies Included in the Systematic Review.pdf

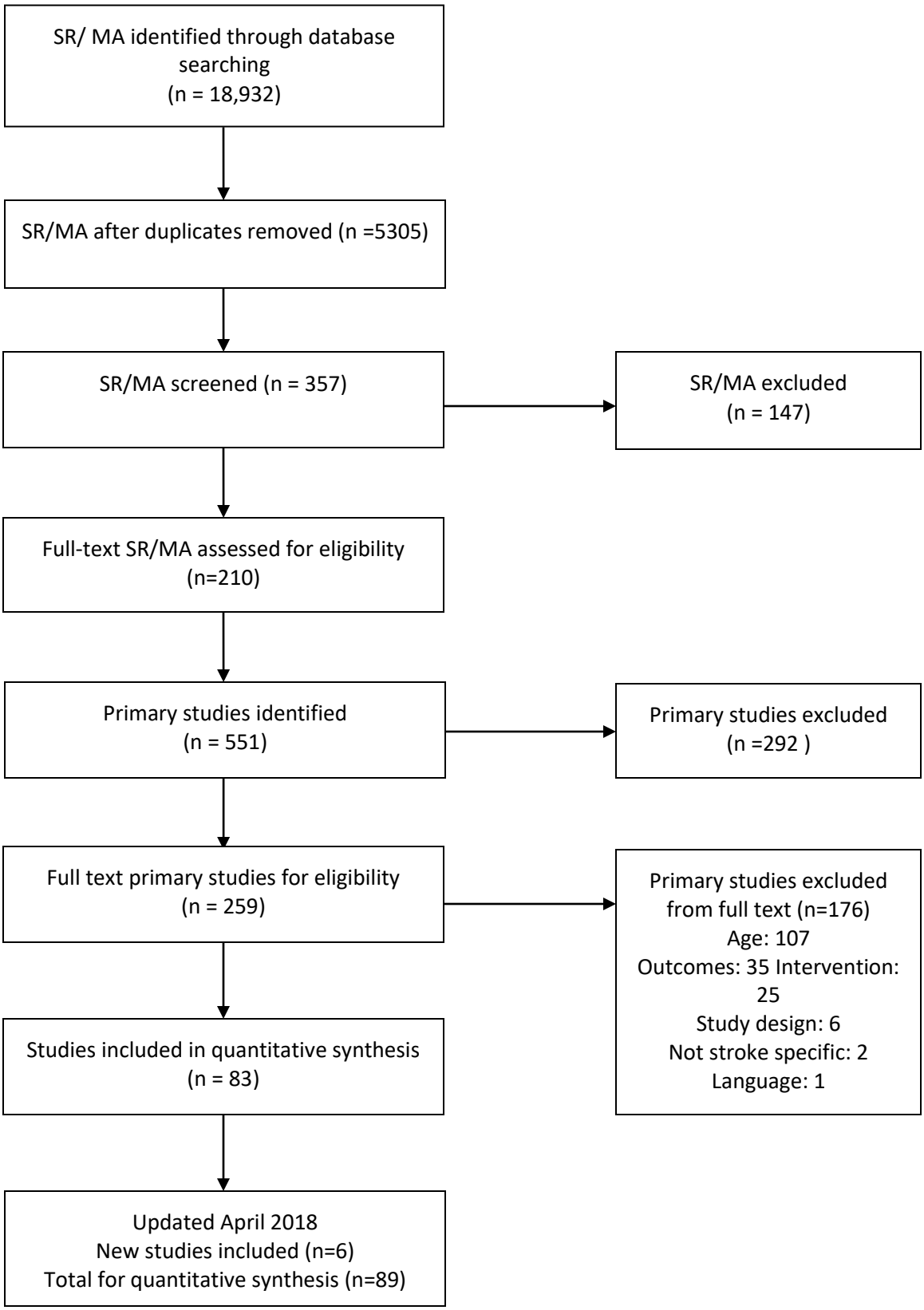
Online Resource 4 Description of All Included Interventions.pdf

Figure 1



MA: Meta-analyses PS: Primary Studies SR: Systematic Reviews

Figure 2



MA: Meta-analyses; SR: Systematic Review